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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/664,970	09/22/2003	Martin Eigenthaler	5281.1666-01	4961

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EXAMINER	
NGUYEN, BAO THUY L	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 05/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/664,970	EIGENTHALER ET AL.	
	Examiner	Art Unit	
	Bao-Thuy L. Nguyen	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25,29-31,35-37,41 and 42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25,29-31,35-37,41 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 3/14/05
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed 14 March 2005 is acknowledged. Claims 26-28, 32-34 and 38-40 have been canceled. Claims 25, 29-31, 35-37 and 41-42 are pending.

2. All rejections not reiterated herein below are withdrawn in view of the amendment to the claims.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 25, 29-31, 35-37 and 41-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 25, 31 and 37 are indefinite with respect to the recitation of "functionally equivalent moiety, mutant, fragment or variant of VASP" because it is unclear if these fragments, for example, would have the proper phosphorylations; or if the mutant and functionally equivalent moiety would have the proper phosphorylations. For example, it is unclear if the fragment of the phosphorylated VASP is phosphorylated at position serine 157 or serine 239.

Claim Rejections - 35 USC § 112, first paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 25, 29-31, 35-37 and 41-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the monoclonal antibody 16C2 that binds VASP as antigen when VASP is present in the phosphorylated form, does not reasonably provide enablement for any other antigen binding protein nor any other monoclonal antibody which recognizes VASP as antigen when VASP is present in the phosphorylated form. Furthermore, the claims fail to comply with the written description requirement because the claimed subject matter was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification, specifically at pages 3, 7, 8, 11, 12, discloses a hybridoma cell line 16C2 producing the monoclonal antibody 16C2 that binds phosphorylated VASP. Specifically when VASP is phosphorylated at serine position 239. Nowhere in the specification is there a description of any other hybridoma producing any other protein or monoclonal antibody that will bind phosphorylated VASP. Although the

specification briefly mentioned that monoclonal antibodies which recognize phosphoserine 157 and phosphothreonine 278 VASP can be isolated using the procedures disclosed for Mab 16C2, it does not give any other detail regarding such a monoclonal antibody nor any characteristics of the hybridoma capable of producing the claimed antibody.

The specification lacks any description of the claimed hybridoma producing the claimed monoclonal antibody and because the deposit of one particular monoclonal antibody (i.e. 16C2), does not enable a monoclonal antibody which may have binding properties that are similar, or which may bind the same antigen because replication of a specific monoclonal antibody is an unpredictable event. Therefore, the claims are not enabled by the specification as filed.

Because the claimed monoclonal antibody has not been properly described and because it is well recognize in the prior art that microheterogeneities (see Harris et al) are common the production of complex glycoprotein such as monoclonal antibodies, it would require undue experimentation for one skilled in the art to make and use the invention as claimed. Furthermore, lacking specific written description in the specification as to the characteristics, physical, chemical or binding properties of any other VASP binding monoclonal antibodies, one skilled in the art cannot make and use the invention as claimed.

In addition, because the specification lacks proper written description of any other VASP binding protein in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, the claims fails to comply with the written description requirement of 35 USC 112, first paragraph.

7. Claims 25, 29-31, 35-37 and 41-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 25, 31 and 37 have been amended to recite a monoclonal antibody that binds VASP only when VASP is phosphorylated at positions serine 157 or serine 239. Such an antibody does not have support in the specification as originally filed. The specification does not provide any description of a *single* monoclonal antibody that can bind to VASP when VASP is *either* phosphorylated at positions serine 157 or serine 239. The specification only discloses monoclonal antibody 16C2, which binds VASP when VASP is phosphorylated at position serine 239.

Claim Rejections - 35 USC § 102

8. The rejection of the claims under 35 USC 102(b) as being clearly anticipated by Adel et al is withdrawn in view of the amendment to the claims. Abel does not teach a

monoclonal antibody that bind VASP *only* when VASP is phosphorylated at position serine 157 or serine 239.

Response to Arguments

9. Applicant's arguments filed 14 March 2005 have been fully considered but they are not persuasive.

Applicant argues that the instant specification provides sufficient disclosure to generate and isolate monoclonal antibodies which are specific for VASP when VASP is phosphorylated at position serine 157 or when VASP is phosphorylated at position serine 239. Post filling evidence in support of this argument shows that using a peptide similar to one disclosed in the specification, a monoclonal antibody, 5C6, is made and shown to bind to VASP phosphorylated at position serine 157. The evidence also shows that monoclonal antibodies, 22E11B8, 22D11D3 and 22E11G10, are also made and shown to bind to VASP when VASP is phosphorylated at position serine 239.

These arguments have been fully considered but are not persuasive. In order to overcome a *prima facie* case of lack of enablement, applicant must demonstrate by argument and/or evidence that the disclosure, as filed, would have enabled the claimed invention for one skilled in the art at the time of filing. Since the evidence submitted is post filling experimentation and post filling publication, such evidence is not adequate to show that applicant was in possession of the full breath of the claimed invention at

the time of filling. In addition, since the members of the genus are indeterminable and widely varying, the showing of 2 members of the genus does not represent the full breath of the genus. Similarly, the showing of 4 members of the genus does not represent the full breath of the genus.

As stated above, the specification lacks any description of the claimed hybridoma producing the claimed monoclonal antibody and because the deposit of one particular monoclonal antibody (i.e. 16C2), does not enable a monoclonal antibody which may be binding properties that are similar, or which may bind the same antigen because replication of a specific monoclonal antibody is an unpredictable event. Therefore, the claims are not enabled by the specification as filed.

Additionally, any evidence submitted to support enablement must be commensurate in scope with the claimed invention, i.e., must bear a reasonable correlation. In the instant case, the evidence submitted is not commensurate in scope with the claimed invention. Specifically, Smolenski teaches that monoclonal antibody 5C6 is specific for serine 157 in its phosphorylated state (paragraph bridging columns on page 25725). In other words, 5C6 binds phosphorylated serine 157. In contrast, the claimed monoclonal antibody is not recited as being specific for either phosphorylated serine 157 or phosphorylated serine 239 of VASP, instead, the claimed monoclonal antibody is recited as binding to VASP when VASP is phosphorylated at positions serine 157 or serine 239. This does not necessary means that the antibody is specific for

phosphorylated serine 157 or phosphorylated serine 239 of VASP. Similarly, Example 2 of the submitted evidence shows monoclonal antibodies which specifically recognize phosphoserine 239 of VASP which does not necessary provide adequate support for an antibody that binds VASP when VASP is phosphorylated at serine 239.

Furthermore, the claims have been amended such that it is now directed to a *single* monoclonal antibody that binds VASP when VASP is phosphorylated at either positions serine 157 or serine 239. The evidence submitted does not provide adequate support for such an antibody. Nowhere in the arguments or prior art references is there a description of a *single* antibody that can bind to VASP phosphorylated at either serine 157 or serine 239. The evidence submitted is drawn to at least 4 different monoclonal antibodies and further state that monoclonal antibodies, 22E11B8, 22D11D3 and 22E11G10 do not recognize other proteins or other VASP phosphorylation sites. Therefore, these monoclonal antibodies cannot bind VASP when it is phosphorylated at serine 157. Only Mab 5C6 can bind phosphoserine 157 of VASP.

Conclusion

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao-Thuy L. Nguyen whose telephone number is (571) 272-0824. The examiner can normally be reached on Tuesday and Thursday from 8:00 a.m. -3:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bao-Thuy L. Nguyen
Primary Examiner
Art Unit 1641
5/18/05